The Stabilities of Meisenheimer Complexes. Part 39.[1] Steric Effects on Rate and Equilibrium Constants for σ-Adduct Formation from Alkyl 2,4,6-Trinitrophenyl Ethers and Ethoxide Ions in Ethanol

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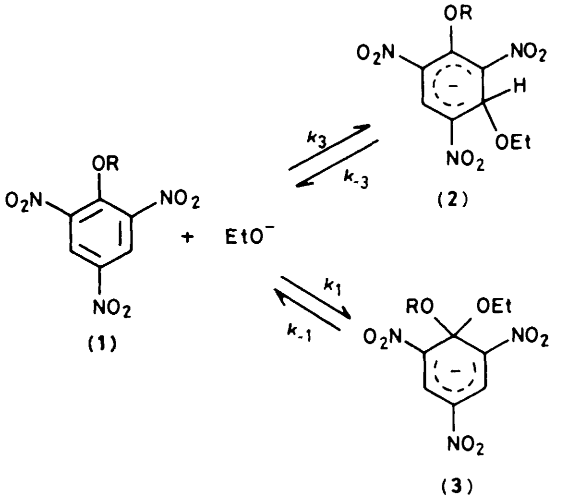
Rate and equilibrium data are reported for reactions of ethoxide ions in ethanol with four alkyl 2,4,6-trinitrophenyl ethers to give isomeric 1,3 and 1,1 σ-adducts. The results indicate the importance of steric factors in this series. Increasing the size of the alkyl substituent causes decreases in values of k_3, the rate coefficient, and K_3, the equilibrium constant, for reaction at the unsubstituted 3-position, and also causes decreases in values of k_1 for reaction at the substituted position.

N.m.r. results show that the initial reversible reactions of alkyl 2,4,6-trinitrophenyl ethers with alkoxide ions yield σ-adducts. Attack at the unsubstituted 3-position is kinetically favoured but the isomeric adducts formed by reaction at the 1-position are thermodynamically more stable.[2-4] The greater stability of the 1,1-adducts has been attributed to the inductive electron-withdrawal of the –OR substituent at the 1-position,[5] the relief of steric strain as this group is rotated from the ring-plane on adduct formation,[2,5] and the stabilising effect of dialkoxy-substitution at an sp^3-hybridised carbon atom.[6]

Although kinetic measurements have been reported for several reactions of this type[7-16] there has been no systematic study of the variations in reactivity when a variety of alkyl ethers react with a single nucleophile in a common solvent. We report here our results for the reactions of four alkyl 2,4,6-trinitrophenyl ethers with ethoxide ions in ethanol which proceed as shown in the Scheme.



Scheme.

Experimental

Alkyl 2,4,6-trinitrophenyl ethers were prepared by reaction of picryl chloride with sodium alkoxide (1 mol equiv.) in the corresponding alcohol. Recrystallisation yielded materials with the following m.p.s; (1; R = Me) 67 °C (lit.,[17] 68 °C), (1; R = Et) 80 °C (lit.,[18] 78.5 °C), (1; R = Pr^n) 41 °C (lit.,[19] 43 °C), (1; R = Pr^i) 95 °C (lit.,[20] 95 °C). AnalaR grade absolute ethanol was used without purification. Sodium ethoxide solutions were freshly prepared by reaction of clean sodium with ethanol under nitrogen and were titrated with standard acid.

Kinetic and equilibrium measurements were made with freshly prepared solutions of reagents using a Hi-Tech SF 3L stopped-flow spectrophotometer. All measurements were made under first-order conditions with the base concentration in large excess over the substrate concentration. Rate coefficients at 25 °C are the mean of five separate determinations and are precise to ±5%.

Results and Discussion

Adducts of structure types (2) and (3) absorb in the visible region and are expected to have rather similar spectral shapes.[4,13] Examination of the systems at 480 nm by stopped-flow spectrophotometry showed the presence of two processes, both colour-forming, with well separated rates. Data are in Tables 1—4. In each case we attribute the faster process to formation of the 3-adduct (2), and with base in large excess equation (1) is applicable. Plots of k_{fast} *vs.* base concentration allowed values of k_3 and k_{-3} to be determined. Combination of these values gave values of K_3 ($=k_3/k_{-3}$) which were in good agreement with those obtained from optical densities measured at the completion of the faster reaction.

$$k_{fast} = k_3[EtO^-] + k_{-3} \qquad (1)$$

$$k_{slow} = \frac{k_1[EtO^-]}{1 + K_3[EtO^-]} + k_{-1} \qquad (2)$$

$$k_{slow} = \frac{k_1[EtO^-]}{1 + K_3[EtO^-]} \qquad (3)$$

The slower process will involve attack at the 1-position, and allowing for the pre-equilibration of substrate and 3-adduct we obtain equation (2). The optical densities measured at completion of the slower process show that even at the lowest base concentration used conversion into adducts (3) is virtually complete. We calculate that values of K_1 are $>10^4$ l mol^{-1} so that under our experimental conditions values of k_{-1} are negligibly small and equation (2) approximates to equation (3).

We recognise that in the presence of excess of sodium ethoxide a third process should be observable involving conversion of adducts (3; R = alkyl) into (3; R = Et). However, the visible spectra of these species should be almost identical[4]

Table 1. Rate and equilibrium data for reaction of 2,4,6-trinitroanisole[a] with sodium ethoxide in ethanol at 25 °C

[NaOEt][b]/M	k_{fast}/s^{-1}	$k_{calc.}$[c]	O.D.[d] (480nm)	K_3[e]/l mol^{-1}	k_{slow}/s^{-1}	$k_{calc.}$[f]	O.D.[g] (480nm)
0.0025	30	30	0.013	95	0.11	0.11	0.066
0.005	35	36	0.022	96	0.19	0.19	0.066
0.010	47	49	0.034	100	0.29	0.28	0.066
0.015	63	62	0.040	95	0.33	0.34	0.066
0.020	74	74	0.046	105	0.38	0.38	0.066
0.030	99	99	0.051	100	0.41	0.42	0.066
0.040	122	124	0.055	106	0.44	0.45	0.066
0.050	149	149			0.45	0.47	0.063

[a] Concentration is 2 × 10^{-5}M. [b] All solutions made up to ionic strength I = 0.05M with sodium perchlorate. [c] Calculated from equation (1) with k_3 2 500 l mol^{-1} s^{-1} and k_{-3} 24 s^{-1}. [d] Measured at completion of the faster colour-forming reaction, with a cell of 2 mm pathlength. Benesi–Hildebrand plot gives a value of 0.068 for complete conversion. [e] Calculated as O.D./(0.068 − O.D.)[NaOEt]. [f] Calculated from equation (3) with k_1 58 l mol^{-1} s^{-1} and K_3 104 l mol^{-1}. [g] At completion of the slower colour-forming reaction.

Table 2. Rate and equilibrium data for reaction of 2,4,6-trinitrophenetole[a] with sodium ethoxide in ethanol at 25 °C

[NaOEt][b]/M	k_{fast}/s^{-1}	$k_{calc.}$[c]	O.D.[d] (480nm)	K_3[e]/l mol^{-1}	k_{slow}/s^{-1}	$k_{calc.}$[f]	O.D.[g] (480nm)
0.0025	32	32	0.010	70	0.051	0.056	0.064
0.005	37	36	0.016	63	0.093	0.097	0.062
0.010	44	45	0.026	63	0.15	0.15	0.063
0.015	51	54	0.033	65	0.20	0.19	0.063
0.020	62	63	0.038	65	0.22	0.22	0.063
0.030	75	81	0.046	73	0.26	0.26	0.063
0.040	101	99	0.049	68	0.29	0.28	0.062
0.050	122	117	0.052	69	0.31	0.30	0.062

[a] Concentration is 2 × 10^{-5}M. [b] All solutions made up to ionic strength I = 0.05M with sodium perchlorate. [c] Calculated from equation (1) with k_3 1 800 l mol^{-1} s^{-1} and k_{-3} 27 s^{-1}. [d] Measured at completion of the faster colour-forming reaction, with a cell of 2 mm pathlength. Benesi–Hildebrand plot gives a value of 0.067 for complete conversion. [e] Calculated as O.D./(0.067 − O.D.)[NaOEt]. [f] Calculated from equation (3) with k_1 26 l mol^{-1} s^{-1} and K_3 67 l mol^{-1}. [g] At completion of the slower colour-forming reaction.

Table 3. Rate and equilibrium data for reaction of n-propyl 2,4,6-trinitrophenyl ether[a] with sodium ethoxide in ethanol at 25 °C

[NaOEt][b]/M	k_{fast}/s^{-1}	$k_{calc.}$[c]	O.D.[d] (480nm)	K_3[e]/l mol^{-1}	k_{slow}/s^{-1}	$k_{calc.}$[f]	O.D.[g] (480nm)
0.0025	36	33	0.008	61	0.050	0.046	0.058
0.005	37	37	0.014	61	0.080	0.081	0.056
0.010	47	46	0.022	58	0.13	0.13	0.057
0.015	55	55	0.029	62	0.17	0.17	0.058
0.020	66	63	0.034	65	0.19	0.19	0.058
0.030	80	80	0.038	58	0.23	0.23	0.057
0.040	95	97	0.042	58	0.27	0.25	0.057
0.050	122	114	0.046	66	0.27	0.27	0.057

[a] Concentration is 2 × 10^{-5}M. [b] All solutions made up ionic strength I = 0.05M with sodium perchlorate. [c] Calculated from equation (1) with k_3 1 700 l mol^{-1} s^{-1} and k_{-3} 29 s^{-1}. [d] Measured at completion of the faster colour-forming reaction, with a cell of 2 mm pathlength. Benesi–Hildebrand plot gives a value of 0.060 for complete conversion. [e] Calculated as O.D./(0.060 − O.D.)[NaOEt]. [f] Calculated from equation (3) with k_1 21 l mol^{-1} s^{-1} and K_3 59 l mol^{-1}. [g] At completion of the slower colour-forming reaction.

and the rate of conversion, governed by expulsion of RO$^-$ from **(3)**, will be slow. Hence this process was not detected by our methods.

It is known that 1,1-dialkoxy adducts **(3)** are capable of complexing cations and that values of rate and equilibrium constants may be affected by such complexing.[12,21,22] Hence we have worked throughout at a constant sodium ion concentration, 0.05M, using sodium perchlorate as the added electrolyte.

The results are summarised in Table 5. Values of the equilibrium constant K_3, for reaction at an unsubstituted ring position, decrease as the substituent is changed along the series H, OMe, OPr^n, OPr^i. The fact that this variation is due entirely to changes in value of k_3 while values of k_{-3} are invariant may indicate that the transition states resemble the adducts rather than the reactants. The electronic effect of alkoxy substituents acting from the *meta*-position is expected to be mildly activating and to be almost independent of the nature of the alkyl group.[23] Hence it is clear that steric effects play the dominant role in this series. Since nitro-groups will exhibit their maximum electron-withdrawing ability when they are coplanar with the ring, factors which inhibit such coplanarity are expected to decrease adduct stability. There is crystallographic evidence for severe steric interactions in 1-substituted-2,4- and 1-substituted-2,6-dinitrobenzenes,[24] and, in particular, in 2,4,6-trinitrophenetole the nitro-groups at the 2- and 6-position are rotated from the ring-plane by 32 and 61° respectively.[25] Although crystallographic data for the other alkyl ethers have not been reported it is likely that steric congestion and rotations of *ortho*-nitro-groups will increase with the size of the alkyl substituent. Adduct formation at the 3-position will not relieve this unfavourable steric interaction.

Reaction at the 1-position will result in relief of steric interaction as the alkoxy substituent is rotated from the ring-

Table 4. Rate and equilibrium data for reaction of isopropyl 2,4,6-trinitrophenyl ether[a] with sodium ethoxide in ethanol at 25 °C

[NaOEt][b]/M	k_{fast}/s^{-1}	$k_{calc.}$[c]	O.D.[d] (480 nm)	K_3[e]/l mol^{-1}	k_{slow}/s^{-1}	$k_{calc.}$[f]	O.D.[g] (480 nm)
0.0025	29	29	0.005	32	0.027	0.028	0.057
0.005	31	32	0.011	39	0.053	0.051	0.057
0.010	36	36	0.018	37	0.090	0.089	0.057
0.015	40	41	0.023	35	0.12	0.12	0.058
0.025	51	51	0.032	37	0.16	0.16	0.057
0.035	60	60	0.036	33	0.19	0.19	0.057
0.050	74	74	0.044	38	0.22	0.22	0.058

[a] Concentration is 2×10^{-5}M. [b] All solutions made up to ionic strength $I = 0.05$M with sodium perchlorate. [c] Calculated from equation (1) with k_3 950 l mol^{-1} s^{-1} and k_{-3} 27 s^{-1}. [d] Measured at completion of the faster colour-forming process with a cell of 2 mm pathlength. Benesi–Hildebrand plot gives a value of 0.067 for complete conversion. [e] Calculated as O.D./(0.067 − O.D.)[NaOEt]. [f] Calculated from equation (3) with k_1 12 l mol^{-1} s^{-1} and K_3 35 l mol^{-1}. [g] At completion of the slower colour-forming reaction.

Table 5. Summary of kinetic and equilibrium data for reaction with sodium ethoxide[a] in ethanol at 25 °C

Substrate	k_3/l mol^{-1} s^{-1}	k_{-3}/s^{-1}	K_3/l mol^{-1}	k_1/l mol^{-1} s^{-1}
(1; R = Me)	2 500	24	104	58
(1; R = Et)	1 800	27	67	26
(1; R = Pr^n)	1 700	29	59	21
(1; R = Pr^i)	950	27	35	12
1,3,5-Trinitrobenzene[b]	33 000	27	1 200	

[a] Measurements with the alkyl 2,4,6-trinitrophenyl ethers were made in solutions of ionic strength 0.05M, using sodium perchlorate as compensating electrolyte. [b] The data, from reference 6, correspond to reaction at an unsubstituted ring position of 1,3,5-trinitrobenzene.

plane. Hence in the 1,1-adduct (**3**) the *ortho*-nitro- groups may approach planarity with the ring.[26,27] This together with the other two factors mentioned in the Introduction accounts for the greater stability of 1,1-adducts than of their 1,3-isomers. Our results do not allow determination of the variation of values of K_1 with substituent but we find that values of k_1 decrease monotonically with increasing size of the alkoxy group. This order reflects the *F*-strain, steric hindrance to approach of the nucleophile, expected in this series.[13,28]

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